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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/648,790	08/28/2000	James L. Hartley	0942.285000C/RWE/BJD	9852

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[REDACTED] EXAMINER

SANDALS, WILLIAM O

ART UNIT	PAPER NUMBER
1636	/ /

DATE MAILED: 10/21/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No. <b>09/648,790</b>	Applicant(s) <b>Hartley et al.</b>
	Examiner <b>William Sandals</b>	Art Unit <b>1636</b>

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1)  Responsive to communication(s) filed on Jul 24, 2002
- 2a)  This action is FINAL.      2b)  This action is non-final.
- 3)  Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

**Disposition of Claims**

- 4)  Claim(s) 52-67 is/are pending in the application.
- 5a) Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5)  Claim(s) \_\_\_\_\_ is/are allowed.
- 6)  Claim(s) 52-67 is/are rejected.
- 7)  Claim(s) \_\_\_\_\_ is/are objected to.
- 8)  Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9)  The specification is objected to by the Examiner.
- 10)  The drawing(s) filed on Jul 24, 2002 is/are a)  accepted or b)  objected to by the Examiner. Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11)  The proposed drawing correction filed on \_\_\_\_\_ is: a)  approved b)  disapproved by the Examiner. If approved, corrected drawings are required in reply to this Office action.
- 12)  The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13)  Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)  All b)  Some\* c)  None of:

1.  Certified copies of the priority documents have been received.
2.  Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3.  Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\*See the attached detailed Office action for a list of the certified copies not received.

- 14)  Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
- a)  The translation of the foreign language provisional application has been received.
- 15)  Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1)  Notice of References Cited (PTO-892)
- 2)  Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3)  Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_
- 4)  Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5)  Notice of Informal Patent Application (PTO-152)
- 6)  Other: \_\_\_\_\_



## **DETAILED ACTION**

### ***Drawings***

1. The drawings as submitted on July 24, 2002 in Paper No. 9, have been approved by the draftsman.

### ***Response to Arguments***

2. Amendments to the claims in Paper No. 10, filed July 24, 2002 have overcome some of the rejections of the claims under 35 USC 112, second paragraph in the previous office action, and those rejections are withdrawn. The rejections which have been sustained are repeated below along with responses to the arguments.
3. Arguments regarding the rejection of claims 52-67 under 35 USC 102 in Paper No. 10 have overcome the rejection of the claims in the previous office action, and the rejection is withdrawn. New grounds for rejection under 35 USC 103 are presented below.

### ***Claim Objections***

4. Claim 52 is objected to because of the following informalities: at line 4, the word "each" should be inserted for better grammatical form. Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 52-67 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claims 1 and 52-67 are drawn to the limitation “*in vitro* or *in vivo*”. “*in vitro* or *in vivo*” is not defined in the instant specification. “*in vitro*” transposition is used in the prior art to mean a transposition reaction which is carried out in cells in a reaction vessel, as well as a transposition reaction carried out where the target nucleic acid and the transposase are not in cells in a reaction vessel. Therefore one of skill in the art would not know the metes and bounds of “*in vitro* or *in vivo*”. As a result the claim is vague and indefinite.

***Response to Arguments***

8. Paper No. 10 asserts that the instant specification provides a clear meaning to the distinction between “*in vitro*” and “*in vivo*”, as well as the intended meaning of the term “*in vitro*” wherein the claimed recombination reaction is done in a test tube, and outside of any cells. Several passages in the specification are pointed out as teaching this type of “*in vitro*” reaction. It is further stated that these cited passages make it clear as to the meaning of the term “*in vitro*”. Since there is a lack of clarity in the prior art, the burden falls upon the instant specification to

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make the distinction, and unambiguously define this term. However, the instant specification at page 35, lines 3-9 teaches an “*in vitro*” reaction done in a test tube with cells. Therefore, there is no clear teaching of the meaning of the term, and the rejection is sustained.

9. Claim 52 contains the trademark/trade name PCR. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a polymerase chain reaction and, accordingly, the identification/description is indefinite.

***Response to Arguments***

10. Amendments to the claims in Paper No. 10 have not removed the trademark/trade name “PCR” from the language of the claim. Therefore, the rejection is sustained.

11. Claims 60, 62 and 64 recite the limitation "mutants thereof". One of ordinary skill in the art would not know how to interpret the metes and bounds of this limitation. A mutation of a recombination site may be closely patterned after the subject recombination site or may be very

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loosely patterned after the subject recombination site, such that it may bear no resemblance or form recognizable as the subject recombination site which may be chemically and/or biologically totally unrelated in function or form to the subject recombination site.

***Response to Arguments***

12. Arguments presented in Paper No. 10 assert that claim 52 provides the assertion that the claimed mutant sites must be functional, thereby averting the rejection. No such language is found in claim 52, therefore the argument is not convincing and the rejection is sustained.

***Claim Rejections - 35 USC § 103***

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 52-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,851,808 (Elledge et al., of record).

The claims are drawn to an in vitro method of cloning a polymerase chain reaction product comprising obtaining a polymerase chain reaction product comprising a first recombination site and a second recombination site which do not recombine with each other and combining the polymerase chain reaction product with a vector comprising a third recombination site and a fourth recombination site which do not recombine with each other under conditions

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such that recombination occurs between the first and third recombination sites and the second and fourth recombination sites thereby making a product vector. The product vector may be inserted into a host cell. The vector may be an expression vector. The vector may contain a selectable marker, a cloning site, a restriction site, an operon, an origin of replication and a gene or a partial gene. The polymerase chain reaction product may be linear. The recombination sites may be *lox* sites, which may be *loxP* or *loxP511*, or *att* sites, or FRT sites. The recombination protein may be Cre.

Elledge et al. taught at columns 17, 18 and 23-26 an *in vitro* method of recombination between a linear DNA and a host vector using a recombinase enzyme to recombine the linear DNA and a host vector to form a product vector. At columns 29-30 Elledge et al. taught the use of a polymerase chain reaction product comprising obtaining a polymerase chain reaction product comprising a first recombination site and a second recombination site which do not recombine with each other and combining the polymerase chain reaction product with a vector comprising a third recombination site and a fourth recombination site which do not recombine with each other under conditions such that recombination occurs between the first and third recombination sites and the second and fourth recombination sites thereby making a product vector. The product vector of the *in vitro* reaction may be inserted into a host cell. The vector may be an expression vector. The vector may contain a selectable marker, a cloning site, a restriction site, an operon, an origin of replication and a gene or a partial gene. The polymerase chain reaction product is

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linear. The recombination sites may be *lox* sites, which may be *loxP* or *loxP511*, or *att* sites, or FRT sites. The recombination protein may be Cre.

US 5,851,808 did not teach that *att* sites may be *attB* sites, *attP* sites, *atttL* sites or *attR* sites, nor that the recombination *att* recombination proteins are Int Xis or IHF. However, it is well known in the art that *att* sites may be *attB* sites, *attP* sites, *atttL* sites or *attR* sites, and that the *att* recombination proteins are Int, Xis or IHF as taught in US 5,354,668 at columns 10-11.

It would have been obvious to one of ordinary skill in the art at the time of filing the instant application to produce the instant claimed invention following the teachings of Elledge et al. because Elledge et al. teaches at columns 17, 18 and 23-26 the *in vitro* recombination reaction using a recombinase, and at columns 29-30, Elledge et al. teach the making of a linear DNA by polymerase chain reaction, where the linear DNA contains two recombination sites which do not recombine with each other, then recombining the linear DNA with a host DNA which also contains two recombination sites which do not recombine with each other, and producing a recombinant product DNA. Elledge et al. make it perfectly clear through these teachings, that one of ordinary skill in the art would know how to recombine a linear DNA produced by polymerase chain reaction with a host DNA vector, to produce a product DNA *in vitro* where the linear DNA and the host DNA both may contain recombination sites which do not recombine with each other.

One of ordinary skill in the art would have been motivated to produce the instant claimed invention following the teachings of Elledge et al. because the Elledge et al. state at column 1,

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lines 55-58 that the method provides a system for the rapid subcloning of nucleic acid sequences *in vivo* or *in vitro* without the need for restriction enzymes. Elledge et al. make it clear that *in vitro* is an equivalent to the previously taught *in vivo* method, thereby making the *in vitro* method a desirable and useful method for the practice of subcloning by one of ordinary skill in the art. Further, a person of ordinary skill in the art would have had a reasonable expectation of success in the producing the instant claimed invention given the teachings of Elledge et al.

### ***Conclusion***

15. Certain papers related to this application are *welcomed* to be submitted to Art Unit 1636 by facsimile transmission. The FAX numbers are (703) 308-4242 and 305-3014. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by the applicant or applicant's representative, and the FAX receipt from your FAX machine is proof of delivery. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications should be directed to Dr. William Sandals whose telephone number is (703) 305-1982. The examiner normally can be reached Monday through Thursday from 8:30 AM to 7:00 PM, EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached at (703) 305-1998.

Any inquiry of a general nature or relating to the status of this application should be directed to the Zeta Adams, whose telephone number is (703) 305-3291.

William Sandals, Ph.D.  
Examiner  
October 18, 2002

  
TERRY MC KELVEY  
PRIMARY EXAMINER